AIR POLLUTION AND HEALTH*

REPORT BY THE
COMMITTEE ON PUBLIC HEALTH
THE NEW YORK ACADEMY OF MEDICINE

I. MORTALITY

Acute Episodes

NEW YORKERS have been menaced by serious air pollution episodes on several recent occasions. As yet, however, the people of this city have not had an experience to compare with those of the Meuse River Valley in Belgium in 1930; Donora, Pa., in 1948; or London in 1952, again in 1956, and a third time in 1962.

The episode in Belgium occurred during the first week of December 1930. A thick fog, arising in part from abnormal weather conditions, blanketed the entire country. The situation was especially marked in the river valleys, notably in a 15-mile section of the heavily industrialized valley of the Meuse River.[1, 2]

Beginning with the third day of the abnormal weather, a large number of people in this section of the valley became ill with respiratory tract complaints. About 60 of them died. The number of fatalities was considered to be about 10.5 times the expected amount under ordinary circumstances for an equivalent period of time and season. The people who died were largely the elderly and those persons with chronic diseases of the heart or of the lungs. Observations in autopsies matched clinical signs in the living. These findings indicated that the probable causative agent was an irritant chemical substance (or group of substances) that acted on the lining of the respiratory tract.

The episode in Donora, Pa., took place during the last week of October 1948. In an interval of 4 days there were 17 deaths in this community. A normal expectation was an average of two deaths in an equivalent period of time. In the days immediately following the episode, there were three more deaths among persons who had become ill during the episode.[3]

Autopsies were done on five persons who had died, three of whom died during the episode, and two later. Of the five, three showed acute irritative changes in the lungs, characterized by capillary dilatation, hemorrhage, edema, purulent bronchitis, and purulent bronchiolitis. A frequent diagnosis at autopsy was chronic cardiovascular disease, the existence of which antedated the episode. This opinion, based on observation of tissue change, confirmed the conclusion previously reached on clinical grounds, that a preexisting heart disease increased the chances of serious illness and death during an air pollution episode.

For 5 days during December 1952, many parts of the British Isles, especially London, were enveloped in a fog associated with abnormal weather conditions and a temperature inversion. The mortality records showed that for a crucial period—one that covered the week of the episode and the week following—there was a total of about 4,000 excess deaths in Greater London compared with

*Approved by the Committee on Public Health, May 2, 1966.

those of a similar period in previous years. Medical opinion attributed the excess deaths to the fog incident.[4]

Nor was the increase in mortality confined to the very old or the very young. Investigation showed that persons of all ages shared to some extent in the increased mortality although the highest increment was among persons 45 years of age and older.

The 1952 episode was so severe and so incited public opinion that the British government called for an investigation. This resulted in a series of recommendations aimed at preventing recurrences. Yet a later episode in the winter of 1956 accounted for 1,000 excess deaths. And in 1962 another fog incident produced an excess of 700 deaths.

New York City has had episodes of air pollution but fortunately the effects have been on a lesser scale. An anticyclone associated with temperature inversion dominated the New York City area from November 12 to 21, 1953. During this period, air pollution—measurable by amounts of sulfur dioxide and smoke-shade—increased and reached unusually high levels as the temperature inversion intensified. Mortality data for New York City disclosed a statistically significant increase in the number of deaths from November 15 to 24.[5] Apparently the increase was generally distributed over all age groups.

In 1963 New York City had another episode.[6] In the 15-day period from January 29 to February 12 it experienced heavy air pollution. During this period there were 647 more deaths than the average for the similar period in years 1961 to 1965. But during that period of 1963 the city had the coldest spell in 10 years and an Asian flu epidemic. When the effect of cold weather and the flu epidemic were excluded statistically by comparison of the mortality figures from 1958 to 1963, when the city experienced cold weather and a flu epidemic but normal levels of air pollution, the total of excess deaths attributable to air pollution became 405.

Almost immediately after the fog lifted in the valley of the Meuse River, a search was made to discover, if possible, the specific causative factor responsible for the deaths and illnesses. After consideration of all the gases and aerosols that had been discharged into the air of this industrial valley, it was believed that only an irritant air pollutant could have caused the deaths. Continued study led to the belief that the excess mortality and morbidity in the valley of the Meuse River was due to a mixture of sulfur dioxide gas and sulfur trioxide aerosol.[1, 2] The role of sulfur dioxide in air pollution has been known since 1600, when new methods of coking coal were being developed to remove some of the sulfur and volatile components from the fuel.

Investigators of the Meuse River Valley episode found, at autopsy, that in the alveoli there were extremely fine particles of pure carbon. Firket points out that certain solid particles cannot have been discharged into the atmosphere in a pure state but must have contained several substances including gases.[1] He observed that while in the state of pure carbon these particles may have been harmless, it is quite possible that they incorporated irritant acids. Taking cognizance of the less soluble gases, or those of lesser specific weight—such as sulfur dioxide—Firket was of the opinion that they pass more easily into the depths of the respiratory pathways. Also significant were abnormal weather conditions permitting the pollutants to accumulate to toxic concentrations.

Following the Donora episode, a study was launched in an effort to deter-

mine the specific substance or substances that might have been the immediate cause of the deaths in this region. But the effort led to an impasse. Based on the information collected after the episode, it was not possible to conclude with certainty that any single one of the measured airborne materials could have accounted for the syndrome. It did appear reasonable, however, to conclude that the adverse effects on health probably were due to a combination of two or more of the contaminants. The culpable agent, the investigators believed, was a combination of sulfur dioxide—together with its oxidation products—and nonspecific particulate matter.[3]

In an official report dealing with the London episode of 1952, the specific etiology was indicated as follows: "While the available evidence does not allow of a clear indictment of any one constituent of the fog, the conclusion is inescapable that the excessive mortality . . . was the result of irritation of the respiratory tract by contaminants." The report adds that the "irritants mainly responsible probably were those derived from the combustion of coal and its products and their lethal effects were almost wholly exercised in persons already suffering from chronic respiratory or cardiovascular disorders."[4]

Subsequent British studies support the view that pollution in that part of the world is attributable overwhelmingly to the combustion of coal and oil, which contain compounds of sulfur as impurities in varying degrees. Smoke and sulfur dioxide are now measured routinely in London and are used as indices of pollution. *It is important for New Yorkers to recognize that these two pollutants are present in roughly the same amounts in London and New York.*[7]

If there is any inclination to regard these episodes, actually major disasters, as rare, it should be noted that both the Meuse Valley and Donora had had somewhat lesser incidents before their crises. Also, from 1873 to 1952 Britain had six similar but somewhat less calamitous crises of severe fogs associated with increase in mortality.[8-12] It is disquieting to some observers there that the disasters are growing larger and more frequent, three in 8 years.

After each of three major episodes similar conclusions were drawn and hypotheses advanced: postmortem examinations as well as clinical observations revealed pathological changes limited to the respiratory tract. They had been produced by an irritant substance. Air pollution intensified by prevailing weather conditions was believed to be the source of the irritants. More than one pollutant was believed to be responsible. Sulfur dioxide, sulfur trioxide, particulate solids, and aerosols as carriers were specifically mentioned as the injurious interacting agents. From this evidence and reasoning it was concluded that air pollution can be lethal. Persons with preexisting cardiorespiratory disease were found to be particularly vulnerable.

Thus, it developed that some 35 years ago an important beginning was made toward the accumulation of evidence, knowledge, clues, and hypotheses on which to base an on-going study of the problem of air pollution.

Correlated Nonepisodic Mortality

After these dramatic fatalities during episodes of air pollution, it was logical to investigate whether a higher death rate occurred during periods of high but less than episodic levels of pollution. Numerous studies have been conducted to ascertain whether air pollution takes a toll even when its level

is not so intense. For this purpose, mortality rates and levels of air pollution during specified periods have been compared. This procedure has been applied with variations. Death from all causes or from a selected category of causes may be measured. Districts with dissimilar degrees of pollution may be compared for their mortality experience expressed in annual rates. Or the comparison may be on a temporal basis with the same population groups. A short period of higher-than-normal levels of pollution may be compared with another period of equal length but lower pollution values to ascertain the excess number of deaths. One or more of the pollutants may be used as an index of gross pollution. Since the finger of suspicion had been pointed to sulfur dioxide as the pollutant probably most responsible for the disastrous effect, in a number of studies the mortality figures were also related to the presence of high and low sulfur dioxide regions.

According to Burgess and Shaddick, "there is little doubt that living in London for a long period of time increases the risk of dying from respiratory disease, particularly bronchitis." In a report published in 1959, Burgess and Shaddick assert that "a significant relationship between mortality and the two types of atmospheric pollutants measured—smoke and sulfur dioxide—has not been demonstrated, though the former looks the more dangerous." They concede, however, that "this does not preclude there being a critical level of one or both in combination that would be directly associated with increased mortality . . . but equally there may be other types of pollutants more dangerous than either."[13]

Hewitt, in a study of mortality in the London boroughs during 1950-52 with special reference to respiratory disease, found that while the total number of deaths was not excessive by national standards, there were in fact some thousands of "extra" deaths among males generally and in particular among those in the 45- to 64-age group. He suggested that the statistics were consistent with the hypothesis that air pollution, besides its well-known short-term effect, exerts an important influence on the long-term death rates from respiratory diseases (especially bronchitis), and a similar influence on the mortality from heart disease.[14]

Pemberton and Goldberg, on their part, found "a significant correlation between the average sulfur dioxide pollution in the county boroughs of England and Wales and the mortality rates for bronchitis in men, 45 years of age and over, for three years: 1950, 1951 and 1952." The report states that the association between solid matter as the index of air pollution and bronchitis mortality rates was much less consistent.[15]

Another investigator who correlated the indices of air pollution in the 83 county boroughs of England and Wales with death rates among middle-aged males from various respiratory and other diseases found a relatively close association between air pollution and death from bronchitis.[16]

Stocks concluded a report of a study by saying that: "When standardized mortality ratios for bronchitis and cancers in the county boroughs of England and Wales are related to the average amounts of undissolved deposit and smoke from the air in those towns, highly significant statistical correlations are found for bronchitis and lung cancer with both types of pollution after eliminating the effects of population density on the correlations."[17]

In connection with the association between certain diseases and air pollution, Gorham reported that he found a highly significant correlation between bronchitis

and the *p*H of precipitation in the 53 county and metropolitan boroughs of England, Scotland and Wales for a 5-year period, 1950-1954.[18]

Fairbairn and Reid, who carried out a study in 37 areas of England, Scotland and Wales from 1948 to 1954 on men and women, ages 45 to 64, found the association of bronchitis mortality with fog indices in both sexes highly significant.[19]

During the period 1890 to 1914, a number of studies on air pollution were made in various cities of the United States. An intense investigation was conducted in Chicago, Ill., about 1910. Other cities surveyed were St. Louis, Mo., in 1907 and Pittsburgh, Pa., in 1912.

As smoke, smog, and dust pollute the air in more and more communities and with increasing concentration, there is a rising incidence of respiratory diseases. Two chronic respiratory diseases in particular, emphysema and bronchitis, constitute a health menace of major magnitude. *These two diseases have been cited in recent reports as the fastest growing cause of death in the United States.*[20]

Between 1952 and 1962, the mortality from emphysema-bronchitis has more than quadrupled, from 3,846 to 15,915. From emphysema alone, deaths are six times higher at the end of the same period, 1,914 to 12,368.

More recently, studies were made in other areas of the United States where the problem of air pollution had become critical. It should be noted that air pollution may differ in its composition as well as in intensity. Its differing nature, which is determined by the source, is exemplified by the contrast between prevailing conditions in Los Angeles, Calif., and in New York City.

Los Angeles' problem is revealed in the constituents that are measured as signals on its alert system: ozone, oxides of nitrogen, carbon monoxide, and sulfur dioxide.

In a report dealing with the problem of air pollution in Los Angeles, Mills stated that "ozone or oxidant-type smog, now known to be formed by the action of sunlight on stagnant inversion of air masses containing unburned hydrocarbons and nitrogen oxides from liquid-fuel motor exhaust fumes, have been present in Los Angeles for more than a decade and are now appearing with increasing frequency in other American cities as the density of motor transport vehicles increases."[21]

Once considered a harmless atmospheric ingredient, ozone is potentially harmful in concentrations above 0.2 ppm, Mills said. His report showed a significant association between the occurrence of smogs in Los Angeles and the day-by-day rises in respiratory and cardiac deaths in the exposed population. Mills concluded that "there no longer exists a reasonable doubt that this smog-death relationship is real and of significant proportions." It should be added, however, that Mills' conclusion has been disputed by California public health officials.

A study carried out recently by Winkelstein and his associates in Erie County, New York, found that mortality increased with increased air pollution in the residence area. Among 5,950 white males, 50 to 69 years old, who died between 1959 and 1961, the standardized mortality ratio for chronic respiratory diseases (3 per cent of all deaths) was 70 per cent for those living in areas of low pollution and 149 per cent in areas of high pollution. The chronic respiratory diseases were classified as emphysema, chronic interstitial pneumonia, asthma and bronchitis, and bronchiectasis.[22]

Air pollution asthma has become one of the major causes of morbidity among U. S. armed forces personnel and their dependents in the Tokyo-Yokohama region of Japan, according to a team of clinicians in the U. S. Army Medical Corps. The disease was incriminated as a significant cause of deaths among armed forces personnel in the region during 1960-1961.[23]

From the evidence it seems incontestable that air pollution in episodes of unusual conditions may produce death.[1-4] High levels of noxious pollutants should not be the sole objects of suspicion. Rapidity of change in concentration during episodes should be borne in mind. It is known that the body adjusts less readily to stress imposed by rapid change in environmental conditions.

Studies indicate that not all deaths seemingly related to air pollution are confined to episodes. It hardly needs to be emphasized that death is as serious and final in a nonepisodic as in an episodic period. Increased death rates when there is no atmospheric incident are interpreted by some experts as a result of a prolonged exposure to a less-than-episodic level of pollution.

The U. S. Bureau of Mines Bulletin 537, containing a bibliography prepared by Davenport and Morgis, lists approximately 400 references on air pollution and health published between 1866 and 1954.[24] Thus, it appears that for 100 years at least, evidence has been accumulating to show that polluted air, in some circumstances, is capable of turning off the breath of life.

II. Morbidity

Acute Episodes

Besides death, the episodes of pollution brought illness on a major scale. In the Meuse Valley disaster the exact number of ill persons was never determined. But it was estimated that thousands were affected, hundreds severely.

Although many aspects of the episode were studied *ex post facto,* the ill were observed and examined at the time. In most cases illness occurred during the third, fourth, and fifth days of the episode and affected persons of all ages and both sexes, including young children. Symptoms common to most of these patients included irritation of the mucous membranes of the larynx and upper airways. Fits of coughing and dyspnea were common, in many cases paroxysmal. Lacrimation and nausea, sometimes with vomiting, were also reported.[2,25]

During the Donora episode in October 1948 approximately 43 per cent of the inhabitants of the immediate area became ill. In 15.5 per cent of the cases the symptoms were classed as mild; in 16.8 per cent as moderate; and in 10.4 per cent as severe. One half of the severe illnesses began before the evening of the third day of the fog, while less than 40 per cent of the mild cases had begun before that time.[3]

There was a relationship between frequency and severity of illness and increasing age. While 43 per cent of the total population reported sickness, 60 per cent of those persons 65 years or over reported some degree of illness. While only 10 per cent of the illness in the total population was severe, about one half of the illness among those persons 65 or over was severe. Cough was the single predominant symptom and occurred in one third of all cases. Dyspnea was the most frequent symptom in the severely ill and its pattern differed completely from that of the cough. Among the more vulnerable persons there was

preexisting disease of the cardiorespiratory system which was judged to be aggravated during the episode.[26]

During the London episode of December 5 to 9, 1952, information on morbidity was scantier than on mortality, hospital admission figures and sick claims give some indication of its extent. The peak of hospital admissions was reached on the fourth day, with 1,100 patients as against only 750 immediately preceding the fog. Four hundred and sixty were admitted with a diagnosis of respiratory disease during the fog episode as against 175 in a previous period. By the end of the week of December 16, sick claims were 9,000 in excess of the usual number.[4]

Morbidity generally had a sudden onset; among many of the severely ill it was on the third or fourth day. Cough was a prominent symptom. The more severely sick were those who had a previous history of "chest trouble," such as chronic bronchitis, asthma, bronchiectasis, or varying degrees of pulmonary fibrosis. Among the clinical signs were cyanosis, moderately elevated temperatures, rales, and rhonchi indicative of bronchospasm. Most of the ill were over 45 years old. Men were attacked with greater frequency than were the women. It was thought that the fog had produced or exacerbated respiratory and, to a much lesser extent, cardiac disabilities.

Points of marked similarity exist between the three major occurrences of air pollution: anticyclonic conditions and thermal inversion were present, accompanied by fog over heavily industrialized geographic areas with like topography. All three occurred during cold weather. This latter point is particularly noteworthy in relation to the London episode where most of the pollutants appear to have originated not so much from industry as from burning of coal used to heat the individual households. It is estimated that 40 per cent, and in winter 60 per cent or more, of all smoke produced in England, including London, results from domestic heating. In all three episodes, investigators of the pollutants appear to agree that there was a high degree of sulfur dioxide and its oxidation products as well as nonspecific particulate matter.[1-4, 26, 27]

New York too has experienced morbidity in connection with episodes of air pollution. The first occurred in November 1953, when air pollution in New York City reached high levels. The impact of this upward swing in pollutants was reflected in a significant increase in visits for upper respiratory illnesses to three hospitals, and for cardiac illnesses to two hospitals. Then during November and December, 1962, New York City reached higher-than-normal levels of intermittent air pollution. At this time, a significant rise in visits for upper respiratory complaints was noted in four old-age homes.[28, 29]

The major episodes also had striking similarities in the illness produced. Symptoms and signs pointed to disorders primarily in the respiratory tract that resulted from an irritant. Those persons with preexisting disease were more vulnerable; therefore, some of the effects on them were frequently interpreted as exacerbation. All these features were in accord with the evidence from the fatalities.

Correlated Morbidity Studies

Since an increase in illnesses and deaths occurred during episodes of air

pollution and increased mortality rates were correlated with high levels during nonepisodic periods, it became important to ascertain whether incidence or prevalence of illnesses rose during noncritical times with their lesser but still higher than normal levels of pollution over a longer period. When extended length of exposure is considered with moderate level of pollution, the possibility of a chronic process may properly be surmised. It is not easily conceivable that an atmosphere that can cause death when highly polluted is without effect when it is less contaminated but continues to be generally prevalent or recurrent. Lesser concentrations of air pollutants have been suspected of having cumulative effects deleterious to health. Consequently evidence has been sought on the effects of repeated exposure to less than lethal concentration of air pollutants over a long stretch of time.

Since most fatal victims during episodes had had preexisting disease, it is desirable to know whether the effect of air pollution during subcritical periods is the worsening of already existing disease, or the initiation of disease in a previously well person, or both. It is not difficult to select the bodily systems and diseases upon which to focus attention. During the episodes, persons with cardiorespiratory disease had been especially vulnerable to mortality, and the clinical pattern of illness indicated involvement of the respiratory tract. It has already been shown that correlation of mortality rates with air pollution exists even during subcritical periods. Prominent among the preexisting respiratory diseases was chronic bronchitis. Accordingly some of the studies on the rate of respiratory illness in regions with elevated but nonepisodic levels of pollutants have concentrated on bronchitis-emphysema.

It is likewise necessary to know what constituents in polluted atmosphere are responsible for adverse effects on health. Because sulfur dioxide has been singled out as a highly suspected lethal component in episodes of polluted air, some studies have been conducted on the occurrence of respiratory diseases in regions of pollution characterized by a high sulfur dioxide content.

It is not enough to know just the identity of noxious pollutants; it is necessary to know the threshold of their irritant effects. In order to protect against illness, not just in episodes, but also in subcritical periods of air pollution, it is necessary to know the level at which a pollutant begins to exert over a long period a pathogenic effect.

In the search for information on these points, correlation of morbidity rates with air pollution levels might yield clues. Despite the theoretical potentiality of morbidity studies, it must be candidly admitted that they are regarded as one of the more difficult types of medical investigation.

In a follow-up of Donora 10 years after, Ciocco and Thompson viewed it as a study of the long-range effects on the health of a population exposed intermittently to varying levels of air pollution.[30] They found that persons who reported acute illness during the episode had higher mortality and prevalence of illness subsequently than did others. Furthermore, persons with complaints of severe acute illness during the episode had greater subsequent mortality and morbidity than those with mild complaints.

It was also concluded that the association between the preexisting cardiorespiratory condition and acute illness during the episode continued into the period of follow-up.

In seeking to ascertain the relative significance of the acute episode and the chronic exposure over the years, the investigators asked: to what extent was greater subsequent mortality and morbidity a direct consequence of the short-term massive exposure; of exposure both before the episode and continued after the episode; or of both? They could not demonstrate that the episode alone had any long-term effects on subsequent health. Nor were they able to relate specific symptoms to particular pollutants.

It will be recalled that during episodes those persons with preexisting cardio-respiratory disease, such as chronic bronchitis and emphysema, were most vulnerable. It was to be expected that in further study of disease entities possibly affected by air pollution, primary interest would be focused on the chronic bronchitis-emphysema group. Bronchitis and emphysema are foremost among a group of so-called chronic respiratory diseases or chronic obstructive pulmonary diseases that includes chronic bronchopulmonary disorders of nonspecific etiologic and clinical features.

Although bronchitis is a disease entity somewhat difficult to define, Pemberton has attempted it: "Bronchitis is a condition in which the sufferer has a chronic cough with sputum lasting for at least four weeks and occurring for at least the previous three winters, which has also resulted in at least one chest illness with one week's absence from work or more and for which no specific cause such as tuberculosis can be found. It is later complicated by emphysema, increasing dyspnoea and ultimately right heart failure." Although this definition may not be unanimously accepted, it offers a concise description of a sometimes vague entity.[31]

Fletcher in 1958 wrote: "In Great Britain we believe that chronic bronchitis is a disease that frequently leads to progressive obstructive pulmonary emphysema which may prove fatal and we regard the syndrome of chronic bronchitis and emphysema as the commonest cause of respiratory disability in our working population." Quite conceivably the term "chronic bronchitis" as used in Great Britain may include a clinical entity called emphysema or emphysema-bronchitis in the United States. As a matter of fact it is asserted that some British physicians believe that many of the emphysema cases in the United States would be called chronic bronchitis in Great Britain.[32]

In the United States bronchitis-emphysema holds a reputation similar to that in Britain. *Here just as it is the most rapidly growing cause of death, it is the fastest rising cause of crippling.*[20] Farber and Wilson in 1958 called emphysema "by far the most common chronic disease of the lungs."[33] In a similar opinion Motley also points out that emphysema is more frequent than tuberculosis, asthma, or lung cancers.[34] Ryder has reported that emphysema is the major single cause of disability having pulmonary origin and occurs more frequently than tuberculosis or lung cancer.[20] Indeed it stands second only to cardiovascular disease as a disabler among males and is responsible for more invalidism in men than other important cripplers such as stroke and cancer.

Fletcher has suggested that atmospheric irritants produce bronchitis which, if in itself not disabling, encourages secondary infection which leads to emphysema with increasing disability. On the pathogenesis of chronic bronchitis he has advanced a hypothesis that he regards as reasonable and fitting most of the facts. He suggests that inhaled irritants including polluted air and cigarette smoke produce bronchial hypersecretion in susceptible subjects. In some of these,

especially in those sections of the population exposed to atmospheric pollution or dusty working environments, secondary recurrent or persistent infection develops and leads to disability from bronchial obstruction and ultimately to pulmonary emphysema.[35]

It is Reid's belief that atmospheric pollution may have some initiating or persistently aggravating effect on chronic bronchitis quite apart from its action during an acute episode on the person with preexisting cardiac or respiratory condition. These views gain import from the increasing incidence of the bronchitis-emphysema disease entity in urban areas. This urban increase is highly suggestive of a link with air pollution.[36]

Significant data on chronic bronchitis in relation to air pollution have been developed in Great Britain.

Figures gathered by the Ministry of Pensions and National Insurance show that miners and foundry workers (both dusty occupations) have a high rate of absence because of bronchitis. On the other hand, agricultural workers have a low proportion of absence due to bronchitis. This fact, according to the author, "may well be due to their freedom from effects of atmospheric pollution."[32]

The long-term study of morbidity among British postmen by Fairbairn and Reid, covering 1948 to 1954, revealed that "severe bronchitis causing permanent disablement . . . among postmen exposed by their job to atmospheric conditions is uniquely related to the frequency of fog and, presumably, to the level of air pollution." Postmen who worked outdoors, but who in all other respects were comparable to other postal service employees who worked indoors, suffered more lost time from work due to bronchitis attacks—with over three times as many absences in the areas of heaviest pollution.[37]

To estimate the immediate effects of a sudden increase in air pollution, Pemberton had a group of about 90 men with known bronchitis keep a daily record (from Nov. 1956 to Nov. 1957) noting whether their condition was better, worse, or unchanged. The records showed that on two occasions when there was a sudden rise in the pollution level, there was a marked increase in the number of men with bronchitis who became more ill, many to the point of incapacitation. To exclude the possibility that this might have been a general nonspecific effect, patients with rheumatoid arthritis were subsequently asked too to keep a similar diary. In this group there was no evidence that a sudden rise in air pollution levels caused pulmonary symptoms. The author thus concluded that "a sudden marked rise in air pollution tended to make our patients with bronchitis worse."[31]

Studies have also been conducted on the relation of air pollution to acute respiratory disease. In a study of the influence of weather on respiratory and heart disease over an 8-year period, Holland *et al.* reported in 1961 a high correlation between respiratory disease and temperature and atmospheric pollution for those aged 15 and over. They present evidence indicating that both atmospheric pollution and low temperature have an effect on the admissions to London hospitals of patients with acute respiratory disease. They state that it is impossible to decide from these data whether pollution or low temperature has a greater effect, but add that apparently each can exert an effect independent of the other.[38]

Dohan has reported a high correlation between the mean concentration of suspended particulate sulfates in the city air and the incidence rates (mean of 3

years) of respiratory diseases lasting more than 7 days in women working in 5 cities. He adds that the age distribution of the population at risk, conditions at work, and social and climatic factors do not account for the fivefold intercity variation in incidence of respiratory disease.[39]

In Norway Skalpe studied respiratory morbidity among 54 workers exposed for extensive periods to SO_2 with concentrations ranging from 2 to 36 ppm in their general working atmosphere. Signs and symptoms of respiratory disease in these workers were compared to those in a group of 56 workers from the same district with similar working conditions but working in an atmosphere free from noxious gases. Both groups were matched for age and smoking habits. A significantly higher frequency of cough, expectoration, and dyspnea on exertion was noted in the exposed group, with the difference greatest in those under 50 years old. The average maximal expiratory flow rate was significantly lower in those workers exposed to SO_2.[40]

The relation of irritant air pollution to bronchial asthma was pointed up by morbidity studies of the three major air-pollution disasters. In those three classical episodes, persons with chronic lung disease, including bronchial asthma, were likely to have become ill. During the Meuse Valley episode signs of asthma were relieved in some patients by adrenaline injections; in others these were quickly followed by cardiac insufficiency and collapse. Donora statistics show that asthmatics, compared with other people, were twice as likely to become ill during the acute episode; further, their illnesses were much more likely to be severe. There can be little doubt that known bronchial asthmatics were strongly affected by the Donora fog. During the London fog of 1952, those with a previous history of chest complaints, including asthma, were among the more severely ill.

Air-pollution asthma has become one of the major causes of morbidity among U. S. Armed Forces stationed in the Tokyo-Yokohama region. More than 100 patients, all stationed in the Tokyo-Yokohama region were studied during 1959 and 1960. As early as 1946, an epidemic of asthmatic bronchitis, termed "Yokohama asthma" was first noted among American troops and their families in this highly industrialized area. The disease attacked otherwise normal, healthy persons between 18 and 40 years of age who had no previous history of asthma and rarely a history of allergy. The condition differed from other known forms of asthma in that it did not respond to the usual medication and most patients showed evidence of marked air-flow obstruction even between attacks and also while taking bronchodilators. An outstanding feature of the disease was its marked tendency to become chronic and progressive. Evacuation from the polluted area resulted generally in disappearance of symptoms in these patients. Further, flying personnel noted prompt relief of symptoms on reaching altitudes of 5,000 ft. or higher, with a return of symptoms often within a few minutes of landing at their base.[23]

Dramatic fluctuations in the daily admission rates for asthmatic emergencies were observed in Charity Hospital, New Orleans, La., between 1953 and 1960. With a mode of 25 admissions per day, admissions on certain days went up to 200. An acute outbreak of asthma in 1958 affected over 100 persons and claimed three lives. The fluctuations and outbreak suggested that some environmental stress might be responsible for this asthmatic response. Accordingly an investigation was undertaken to determine whether air pollution might have been involved.

Since the asthma outbreaks were associated with low wind speeds from the south and southwest, it was assumed that some air contaminant was involved and this pollutant was probably localized not far from the area where most of the afflicted who sought emergency treatment were housed. An area of 24 city blocks in the southwest section of the city was designated for intensive study. A pilot study in July 1960 revealed that in households in that area, 4 per cent of the population were susceptible to asthmatic attacks; and that between 50 and 80 per cent of these had had asthmatic attacks within the past year. Eighty-four adult asthmatics from this area were evaluated by clinical and laboratory methods. These studies revealed no feature to distinguish this group from asthmatics who regularly appear in allergy clinics.[41]

When the concentrations of various air pollutants were compared with asthmatic outbreaks, statistically significant relationship was found between daily asthma emergency clinic admissions and the prevalence of one air pollutant—a poor-combustion particle with associated silica, in most instances larger than 4 μ. Samples taken at one city dump in the summer of 1961 revealed large quantities of this particle. No relationship was shown between concentrations of other pollutants and the number of reported asthma attacks.

It was theorized that either the poor-combustion particle with associated silica produces asthma, or that it travels in consort with asthma-producing agents. Since publication of that report, another acute episode of New Orleans asthma occurred in October of 1962. This outbreak claimed 9 lives in 1 week, and 300 persons sought emergency treatment.

In a study on bronchial asthma and sulfur dioxide in Nashville, Tenn., Zeidberg, Prindle, and Landau reported in 1961 that in 49 adults of a series of 84 patients the asthmatic attack rate varied directly with the level of sulfation in their residential environment. Attack rates on days with the highest (0.042) and lowest (0.000) sulfur dioxide values were significantly different. When the attack rates were shifted over 1 day to take account of possible delayed effects, the differences were even more significant. Wind velocity showed an inverse relationship to the attack rates.[42]

Studies of this kind have indicated that respiratory patients experience discomfort and difficulty that is precipitated by an adverse atmosphere. As stated in the report of the National Conference on Air Pollution in Washington, in 1962, *"The evidence is overwhelming that air pollution contributes to the pathogenesis of chronic respiratory disease."*[43]

Los Angeles County, keenly aware of air pollution in relation to health, has instituted an alert system for excessive amounts of the following pollutants in the air: ozone, oxides of nitrogen, carbon monoxide, and sulfur dioxide. In an effort to determine whether air pollution affects health, the authorities turned to physicians in the community. A questionnaire was circulated among the members of the Los Angeles County Medical Society. More than 50 per cent of the 4,700 physicians queried responded. Most of the respondents stated that Los Angeles smog causes eye and nose symptoms. And the majority added that smog affects the throat and lungs. However, no quantitative data were made available.[44]

Another opinion regarding the effect of air pollution on health came from a survey of pupils and teachers following a smog episode in Los Angeles during October 1954. According to the school officials, all schools in the heavy smog

area reported a substantially increased incidence of headaches, coughs, eyestrain, excessive nasal discharge, and similar problems. There appeared to be a widespread belief that air pollution in the Los Angeles area interferes with school performance and leads to disturbed behavior. Children were said to be irritable, and teachers discontented and frustrated.

To determine the effects on health of atmospheric pollution in New York City, a group of investigators from Cornell University Medical College selected by stratified random sampling technics a representative group of 950 persons representing the major racial, ethnic, and income groups within a half-square mile of Manhattan. Participants remained in the study for one year; during this time they recorded any symptoms daily. They were interviewed once a week.[45]

The usual levels of urban air pollution were not expected to result in readily recognizable disease in this group of normal persons. Health effects, if any, were rather presumed to be subtle, and perhaps expressed through a variety of different pathways. Surprisingly, however, a sudden brief 3-day appearance of symptoms was reported by the members of the study group. Computer analysis of this symptom peak strongly suggested a population response to some environmental challenge.

During this period of symptom peak, SO_2 levels were only slightly higher than those frequently reported at the sampling station, but there was a distinct and abrupt change from a previous low level. This finding suggests that the actual level of pollutants—given a period of adaptation to even high levels—may not be of as much importance as the rate of sudden change.

Symptoms reported during this peak period were rhinitis, cough, sore throat, headache and eye irritation, all considered by 20 per cent of the study population to a "common cold." The investigators, however, considered an infectious etiology incompatible with such a brief period of symptoms in a population of this size.

The Cornell study further revealed that during 1963-64 there were several thermal inversion periods in New York City. One of these occurred October 10 to 27, 1963, when meteorologic conditions—with the exception of high temperatures with less pollution due to space heating—were similar to those in the November-December episode of 1962. For most of the 10-day period of most intense inversion, SO_2 levels remained at 0.25 ppm or greater. They frequently exceeded the California ambient air quality standards which impose a safety threshold of 1.0 ppm for 1 hour or 0.3 ppm for 8 hours. During this period there was a prevalence of the same symptoms as those noted in the previously described episode with a close correlation between symptoms and levels of pollution.

In another series, McCarroll *et al.* studied a "reasonable cross section" of New York City residents for effects of air pollution. Computer data analysis was based on the daily illness experience for 1 year of 1,090 adults, excluding those with chronic cough and those under 15 years of age, all living within a half-square mile area of reasonably homogeneous air pollution. Two symptoms which might be expected to have some relation to air pollution were selected for analysis—cough and eye irritation. Sulfur dioxide and particulate density were used as indicators of the levels of air pollution to which the population was exposed.[46, 47]

Results seemed to indicate that the environmental influences represented by

SO_2 have an immediate effect in producing eye symptoms, and that there is a delay in the production of cough. Similarly, particulate density appears not to contribute to the production of eye symptoms, but does appear to contribute to the production of cough. This is consistent with other evidence that the production of eye irritation is an immediate effect of some pollutants, but that a time lag may be necessary in the production of any but irritative cough.

For a long time, the evidence that air pollution had an influence on morbidity depended on the presence of overt disease with symptoms and clinical signs. About 15 years ago, however, investigators began to consider that a truer indication of the number of persons affected by air pollution and the progression of changes they were experiencing would be possible if the subclinical effects were detected and studied. Underlying this concept was the recognition that there are early stages in the development of the disease or a low-grade chronic process that are below the level of clinical manifestations. Accordingly, investigators began to refine and make more sensitive the method for detecting demonstrable effects of air pollution on the respiratory system.

In 1952, Motley described improved techniques and apparatus for measuring pulmonary function. He suggested that an accurate evaluation of the degree of pulmonary function impairment could be made from a series of physiological tests: 1) ventilation measurements from spirogram tracings—total vital capacity, 3-second vital capacity, maximal breathing capacity, and the shape of the exhalation curve following a deep breath; 2) the degree of bronchospasm present; 3) the residual volume and alveolar nitrogen per cent after 7 minutes oxygen breathing; 4) the arterial blood oxygen saturation at rest and immediately after step-up exercise; 5) oxygen uptake during step-up exercise; and 6) the character and duration of dyspnea after step-up exercise.[48]

In about 75 per cent of the group under study by Motley, the ventilation factor was correct in predicting the degree of pulmonary function impairment as compared to an evaluation based on comprehensive studies including arterial blood and respiratory gas analysis. In a subsequent investigation he found that spirogram tracings were useful as screening tests of pulmonary function to detect early lung function abnormalities even before subjective or roentgenologic changes were apparent.[49]

In discussing the question of respiratory health, Spicer warns that in itself it is not a simple concept. He asserts that respiratory health has different meanings for different investigators. Reporting on a study of pulmonary function in normal subjects and individuals with respiratory abnormalities, Spicer reveals that both patients and normals react together to air pollution, apparently to something in their common environment. He points out that patients who are clinically similar may be different physiologically. "We do not know whether this reaction is causing disease or aggravating existing disease," he says. "Nor do we know whether it is due to factors in the community or in the home environment."[50]

In 1959 Prindle and his associates carried out a study of pulmonary function in two neighboring Pennsylvania communities with widely different air pollution levels. The study involved persons 30 years of age and over in both communities. The tests included lung-volume measurements as well as Average Airway Resistance. An interim finding reported by the Prindle group was that statistically significance differences in Average Airway Resistance and Airway Resistance x

Volume were found between the two communities for either sex, even after differences in height and age were taken into account.[51]

"When viewed in proper perspective," the Prindle report comments, "it appears that this study demonstrates the feasibility of community-wide surveys of pulmonary function with complex instrumentation usually reserved for hospital use." It should be added that this procedure has equal applicability in experimental studies.

In sum, the results of the morbidity studies seem to warrant these conclusions: lesser concentrations of air pollution do affect health adversely; whether air pollution causes a disease de novo, that is, initiates the pathogenic process, is indecisive; there is some evidence that it lowers body resistance, but no chronic process has been recognized that can be said with certainty to be air-pollution disease; thus far the morbidity studies offer no additional clues linking specific symptoms to particular pollutants. It is especially important to note that observations on morbidity are in agreement with those in mortality studies, that air pollution can aggravate preexisting cardiorespiratory disease.

III. Experimental Studies

So dramatic were the episodes of air pollution with illness and death, that they attracted attention, aroused concern, and stimulated a course of inquiry that is still continuing.

After the Meuse Valley incident, evidence was analyzed, conclusions were drawn, clues were derived, and a hypothesis was advanced. They were put forth shortly after 1930 and are still held.

These were the conclusions and postulations:

1) The pathological effects on the body were localized and limited to the respiratory tract.

2) Categories of persons most vulnerable to episodes of air pollution were identified. Preexisting disease of the cardiorespiratory system appeared as the single significant common factor among the fatally ill. Chronic bronchitis was prominent as the preexisting disease in fatal cases. Older persons were more vulnerable.

3) Emphasis was placed on meteorological conditions among the attending circumstances.

4) From the effects of irritation it was postulated that the cause was airborne irritant substances. In specifying in detail the causal complex it was held that: *a*) irritant air pollution was culpable; *b*) not one but two or more pollutants were responsible; *c*) there was interaction of several components: sulfur dioxide, sulfur trioxide, particulate solids, and aerosols as carriers.

Similar conclusions were reached upon analysis of the Donora and London episodes.

Thus, 35 years ago the groundwork was laid for continued studies. The episodes furnished leads and clues which have since been followed. They were the starting point for an intensified investigation into the hazards of air pollution.

To justify the need and desirability of clean air on the basis of conserving health and life requires evidence. It would seem that the acute episodes have provided ample, convincing evidence to answer the question about the influence of air pollution on health and life. Much of the mass of data has been presented

here to demonstrate incontrovertibly that air pollution is indeed harmful to health and dangerous to life.

Besides justification for clean air there is a problem, of course, of action. Obviously, to take steps to remove or lessen air pollution requires sound information and detailed knowledge. For air pollution is a complex of numerous components. To remove any jeopardy from air pollution it is necessary to identify its injurious components and to ascertain their minimum irritant and toxic concentrations.

Thus, to pursue an effective course of action towards removing air pollution raises three fundamental questions: 1) What is the nature of the injurious effects on health and danger to life as shown by disease and symptoms? 2) Which of the components in the causal complex are responsible for injury and danger? 3) At what concentrations do these pollutants begin to exert their injurious effects?

To these questions the evidence from the episodes furnished clues and hypotheses, not definitive answers. They were not known then nor are they known now. No entity has been recognized that can be said with certainty to be air-pollution disease. There is as yet no accurate evidence linking specific symptoms to particular pollutants. It is not known exactly how many and what substances in the air should be regarded as culpable toxic agents nor the levels at which they become injurious.

These questions, with answers as yet unknown, are interrelated. But broadly, the investigation into the hazards of air pollution has moved in two directions. First, in the relationship of air pollution to health and life, there are many missing details about the effects. It should be noted that man is exposed to several kinds of polluted atmospheric conditions. It is sometimes difficult to separate the effects of air pollution by source: occupation, community, and personal smoking. Then too, it is desirable to know the nature and scope of the injurious effects of air pollution on the body. It would be helpful to learn whether air pollution as a major contributory factor is responsible for the origin and progression of a pathogenic process and disease entity, or whether its effects are limited to aggravating and progressing a preexisting disease. Furthermore, inasmuch as persons differ in their sensitivity and susceptibility to atmospheric pollution, variations arise in the response of individuals under the same environment.

It is also essential to ascertain the effects of long-continued exposure to elevated but nonepisodic levels of air pollution. It has been reasoned that it is possible, if not probable, that prolonged exposure to high but less-than-episodic concentrations might have pathogenic effects, that noncritical periods might likewise be responsible for illness and death. As a corollary, it would become necessary to recognize the manifestations of a chronic process.

The second direction of inquiry has been to determine the constellation of conditions and substances in air pollution and their injurious levels responsible for illness and death.

Evidence on these questions has come from two sources: one, the correlation of mortality and morbidity rates with levels of air pollution has already been presented. But evidence has been gathered from still another source, experimental studies. This approach is particularly helpful, if not indispensable, when a relationship is complex and contains many variables.

Experimental reproduction of a disease permits study of its characteristics

and provides solid evidence on causation. For these reasons, the experimental approach facilitates study of the relationship between pollution and man. Unfortunately, the effects of pollution cannot be said to have been completely and faithfully reproduced in man by experimental means. When reproduction of disease is not possible, then the induced aggravation or improvement in the naturally occurring disorder is the next best experimental evidence. It is to be noted that Waller and Lawther found a close association between the clinical condition of a group of 180 patients with chronic bronchitis and emphysema living in the Greater London area and the concentration of atmospheric pollution measured in the city.[52, 53] Farber and Wilson observed a pronounced correlation between the sporadic air pollution of San Francisco, Calif., and exacerbation of symptoms in emphysema.[54] Motley and his co-workers likewise found that smog increased the severity of emphysema.[55] In emphysematous persons the volume of residual air may be increased by bronchospasm and bronchial edema. Breathing of polluted air induced these changes in patients, but exposure for 2 or more days was required to attain the maximal effects.

When 46 patients with emphysema were allowed to breathe air filtered through activated carbon for not less than 40 hours they showed significant improvement as evidenced by decrease in the volume of residual air.[55] As in the adverse change, so in the favorable response there was a period of delay.

It has already been noted that illness appearing during episodes has been characterized clinically as respiratory distress with progressive cardiovascular difficulty. Postmortem observations suggested that changes had been produced by inhalation of an irritant substance. But the irritant is still unknown.

Pollutants comprising air pollution are numerous, and they vary in kind, concentration, and effect. Added to this complexity are variables introduced by changes in weather. There are, moreover, the possible differing effects of air pollution on bacteria and viruses and on their host's resistance. Finally, length of time of exposure is an important variable; particularly in relation to concentration of the pollutant, it assumes utmost importance.

This complex of variables with their relationships and interrelationships must be disentangled if fundamental and vital questions are to be answered. What pollutants in the air are harmful to man? When they operate in multiple, is the effect additive or synergistic? What category of persons by age and state of health are most sensitive to air pollution? Does constant or repeated exposure to low concentrations of pollutants conduce to a chronic process? To obtain more precise information that would answer these practical questions, the experimental method under simplified and controlled conditions with variables limited has been applied.

Unfortunately, during an incident of lethal fog, the atmosphere has not been adequately sampled. It is difficult to plan experimental work on the toxic effects of polluted fog without knowing its composition and the concentrations of its constituents. Data on the acute episodes were reviewed *ex post facto*. In Britain, fog, low temperature, sulfur dioxides and solids in smoke were most often identified as probably responsible for illness. But causation was not definitely, specifically, and completely established.[3] Los Angeles' suspicions are revealed by the list of pollutants on its alert system: ozone, oxides of nitrogen, sulfur dioxide, carbon monoxide.[55]

Those pollutants most under suspicion for injurious effects, as well as other pollutants, have been studied experimentally. But in the absence of precise knowledge of their concentration and physical state in an acute state of smog, the value of the experimental observations is limited to indicating which contaminants are potentially dangerous at specified concentrations.

Of the various pollutants, the effects of sulfur dioxide on both man and animals have been especially studied. It has been demonstrated in experimental studies that irritant gases can have severe effects upon the lungs.[56] At a level found not infrequently in the air, inhalation of sulfur dioxide by animals and man can produce temporary bronchiole spasm; at higher concentrations it leads to increased mucus production; at still higher concentrations it leads to inflammation and sloughing of the superficial epithelium. Sulfur dioxide has been found therefore to be deleterious both for persons in good health and for those with preexisting pulmonary conditions.

As for the effects of prolonged exposure to sulfur dioxide at low levels, it should be especially noted that animals subjected for months to daily inhalations develop fibrotic thickening of the walls of their bronchioles. There is a striking similarity in these changes to those found in the early stages of bronchitis in man.[56]

The accepted permissible limit for prolonged exposure to sulfur dioxide is 5 ppm by volume, a level readily detectable by most individuals.[57] Lawther has reported audible signs of bronchospasm during inhalation of 10 ppm of sulfur dioxide.[58] According to Greenwald, very few healthy adults found concentrations of sulfur dioxide up to 5 ppm objectionable.[59] Concentrations twice as great were apt to be irritating. Frank has reported that there is no significant increase in pulmonary flow resistance at a 1 ppm concentration of sulfur dioxide.[60, 61] But at 5 ppm and higher the flow resistance was elevated, the increase being greater at the higher levels.

It should be noted that most of the experimental work on sulfur dioxide has been at concentrations higher than those reported or estimated during the episodes. It is this disparity of the effects of sulfur dioxide experimentally at low concentrations and the profound effects of air pollution during the episodes that has led to investigation of pollutants beyond sulfur dioxide.[62]

In the respiratory passages production of mucus and whiplike action of cilia exert a significant protective action on the surface membranes of the tracheobronchial tree.[63] When a highly irritant gas reaches the membranes, it will paralyze the cilia, even slough the surface membranes.[63-66]

Another protective mechanism against irritant gases has been suggested. Upon inhalation, gases that are water-soluble may be dissolved in fluids of the upper respiratory tract, and thereby their action is concentrated in this more resistant part of the tract. But this dissolved gas can be modified by aerosols in the inhaled air. Airborne liquid and solid particles can cause the gases to have a much more serious effect. A gas that usually would not reach beyond the trachea may be carried by aerosols, if sufficiently small, to depths of the lungs that it would not otherwise reach. There it is released to wreak its injurious effects.[60, 67-78]

It is apparent that particulate matter has not gone unnoticed as an object of study although the magnitude of a complete undertaking would be enormous. Schepers has declared: ". . . about 3000 chemical particles have been identified

which can be dispersed in air, less than 10 per cent of these we know something about and less than 1 per cent of that which we know is relevant."[79] Smoke and dust are among the more common and better known examples of particulate matter.

Besides this deeper descent into the pulmonary region, another set of circumstances conduces to injurious effects. In the presence of water vapor, sulfur dioxide may be oxidized to sulfur trioxide; the latter is the much stronger irritant. The two gases may form sulfurous and sulfuric acids respectively. Sulfuric acid mist increases airway resistance, and produces bronchitic symptoms.[62, 80-84] The larger the particle the more severe the symptoms. It should be noted that in Pittsburgh, even with a low level of sulfur dioxide, levels of sulfate particles were found in the air at concentrations that experimentally can produce airway disease.[85]

When two or more irritant gases or aerosols are present in the inhaled air their total effect may be the same, greater, or less than the sum of the individual effects. When greater, it is said to be synergistic.[69-72] Exposure to low levels of both sulfur dioxide and trioxide simultaneously has disclosed a marked synergistic effect.[75, 86] Increased significance is imparted to this relationship by the finding of sulfur trioxide as well as sulfur dioxide associated with fog in some urban areas.[87] Pattle and Cullumbine have reported synergism between smoke and sulfur dioxide.[84]

In contrast to the composition of pollution in London, the type in Los Angeles contains little coal smoke, fog, or sulfur dioxide.[88] Auto exhaust gases are the principal source of pollution. Photochemical reactions between volatile organic compounds, especially olefinic hydrocarbons, and the exhaust of nitrogen produce highly reactive peroxy-compounds and ozone.[89-93]

Guinea pigs exposed for 1 to 4 weeks to auto exhaust at a concentration several times higher than the usual, were found to be especially susceptible to severe pulmonary disease.[94, 95]

Irradiated exhaust is chemically similar to photochemical smog and contains oxides of nitrogen, ozone, hydrocarbons, and oxidants. It is chemically different from nonirradiated exhaust. During an epidemic among test animals, significantly higher mortality occurred in those exposed to irradiated exhaust than to non-irradiated exhaust or to pure air.[94]

Animals exposed for only 2 hours to nitrogen dioxide at levels similar to those occasionally found in community atmosphere were found to be much more susceptible to infection by pneumonia organisms.[96] These results are similar to the effects of exposure to irradiated exhaust.

When nitrogen dioxide is given to animals at levels higher than prevail during ordinary periods, it produces pulmonary edema followed often by death.[97] At lower levels over prolonged periods, proliferative changes in bronchial and bronchiolar epithelium with narrowing of passageways leading to a vesicular emphysematous state were observed.[98]

Mice exposed to inhalation of carbon upon which nitrogen dioxide was adsorbed developed focal lung lesions. Carbon was regarded as an example of a carrier whereby high local concentrations of nitrogen dioxide in the lungs were achieved.[78]

Exposure of a healthy man to ozone in concentrations of 2 ppm for 2 hours produced constrictive chest pains, reduction in vital capacity, and prolongation of

exhalation.[99] Repeated inhalation of ozone by animals at a concentration of 1 ppm, only slightly higher than that existing in some urban atmospheres, produced bronchitis and bronchiolitis.[96, 100, 101] Animals subjected for months to daily inhalations of ozone at low levels developed fibrotic thickening of the bronchiolar walls similar to that found in the early stages of bronchitis in man.[56] These effects, it will be recalled, were also seen with prolonged exposure to sulfur dioxide.

For the sake of completeness, it should be mentioned that the possible influence of polluted air, especially its content of polycyclic aromatic hydrocarbons, on the pathogenesis of lung cancer has also been investigated. Kotin has listed six strands of evidence to suggest that the carcinogenic properties of polluted urban atmosphere provide at least two links in the pathogenesis of lung cancer: 1) the environmental presence and entry into the host of experimentally proved carcinogenic agents that epidemiologically have been associated with increased liability to the development of lung cancer; 2) occurrence in the atmosphere of host-modifying factors that facilitate admission, deposition, abnormal retention, and subsequent release of carcinogens with significant increase in their local concentration after liberation. He has qualitatively denoted the existence of a carcinogenic hazard in polluted air.[102] But, as he points out, measurement or even quantification of this hazard independent of other environmental menaces is difficult if not impossible. It is hard to evaluate the relative influences of air pollution and smoking. But he asserts flatly that eliminating polluted urban air would result in a reduction in the incidence of lung cancer.

Wynder regards it as an established fact that the urban population has a somewhat higher rate of lung cancer than does the rural population.[103] But this so-called urban factor has not been identified; hence there is no proof that air pollution is or is not the urban factor. Despite his somewhat more restrained position, Wynder holds that inasmuch as experimental studies have revealed several factors that contribute to the induction of cancer, the reduction of pollutants in the atmosphere is to be desired.

Carbon monoxide has long been under suspicion inasmuch as its lethal effects in high concentrations are well known.[104] But there is not complete agreement about chronic effects arising from prolonged exposure to sublethal or lesser concentrations. When inhaled, carbon monoxide combines with the hemoglobin in the blood to form carboxyhemoglobin, which diminishes oxygen transport in the blood.[105] Inasmuch as gasoline-engine exhaust is a principal source of carbon monoxide, data have been gathered on its concentrations in the air of streets and on blood carboxyhemoglobin of persons with increased exposure under various circumstances to the gas.[106-109] But the evidence of demonstrable ill effects has not been conclusive. Nevertheless, one school of thought points out that relatively low concentrations of carboxyhemoglobin can produce small but definite interference with oxygen transport.[110, 111] Persons with borderline circulatory disturbances could be seriously affected, even jeopardized.

The toxicity of lead has long been recognized by the public under the term "lead poisoning." At one time much of the source of lead was from paint, but with its omission from that product and its introduction into gasoline, watchful eyes shifted to the air.

Of the several portals of entry, the respiratory tract is the more dangerous because inhaled lead dust may enter rapidly into the circulation and so become

widely distributed. Lead poisoning is nearly always chronic because absorption usually proceeds slowly. Of all the pollutants in the air, its deposition in the body, its cumulative effects and its formation of a chronic process are perhaps best known.

Most persons have measurable amounts of lead in their bodies. The levels in the blood and urine are an index of the degree of absorption associated with an exposure. It became important to establish the values for normal lead in the blood in order to evaluate properly the content under conditions of exposure. Because intense exposure can result in high values that rapidly decline as the lead is distributed to the soft tissues and skeleton, these high levels may be unassociated with symptoms of poisoning. Kehoe has stated that ". . . conclusive evidence of abnormal lead absorption should not be given more than its proper weight. Lead absorption is not synonymous with lead intoxication. . . ."[112]

Recently conducted was a survey of lead in the atmosphere of three urban communities: Cincinnati, Los Angeles, and Philadelphia.[113] Its purpose was threefold: 1) to establish a baseline for the lead content of the atmosphere in urban areas and in the blood and urine of selected population groups; 2) to ascertain whether differences exist in levels of lead in the blood and urine of individuals exposed to different amounts of lead in a community atmosphere; 3) to obtain data that would permit review of the potential harmful effects of existing lead concentrations in the atmosphere on the general population or segments of the population. Data from the National Air Sampling Network in Cincinnati had shown no consistent trend in the concentrations of lead in the atmospheres of the three cities during the past 5 years.

In the survey, concentrations of lead in all three cities were found to be higher in their downtown and industrial areas than in their outlying areas. Noted was a trend toward an increase in the concentration of lead in the blood of the groups of persons as they varied in their places of residence and work from rural to central urban areas. There was about a fourfold difference in values between the rural and central urban groups according to the concentration of lead in the atmosphere to which they were exposed. But these differences were well within the presently accepted range of lead levels for humans and were said to be not significant in terms of a threat of occurrence of lead intoxication within the groups.

Reassuring as these findings may be, they do not completely dispel all concern. If automotive vehicles continue to increase in number at the present rate and reach predicted figures, and if they are propelled by lead-containing fuel, the possibility of unsafe levels of lead in the air should not be overlooked. It is this contingency that calls for continued watchfulness and surveillance of the content of lead in the air and in the blood of exposed persons.

What Minot had to say in 1938 about the physiological effects of small amounts of lead seems equally pertinent today:[114]

> . . . it is apparent that the recognition of the harm done by the small amounts of lead absorbed by the average individual is bound to be difficult. The investigations which give evidence of the marked influence of lead in great dilution on various isolated tissues incline one to the view that the continuous absorption of any amount of lead must result in less than optimal conditions for the organism as a whole.

> At present, however, we do not know what to look for in the average individual as subjective or objective manifestations of this slightly unfavorable condition. From the available estimates of the present lead exposure and the amount absorbed by the average individual, it appears doubtful that the usual recognized signs and symptoms of plumbism are to be expected in more than an occasional highly susceptible person. There may conceivably be many instances in which lead is contributing to constipation, or to a tendency to anemia, to ready fatigability of muscles, to hypertension or to impaired nervous and mental function. There are, however, many other possible causes of exactly the same abnormalities. . . .
>
> . . . Probably the question of greatest concern at present is whether modern practices are going to result in a gradually increasing lead exposure for the average individual. . . . There is no doubt, as was stated at the beginning of this paper, that the continued absorption of amounts of lead which are still relatively small result in outspoken poisoning. It is important, therefore: 1, to keep informed as time goes on as to the margin of safety which we have between the lead exposure of the average individual and those amounts generally recognized as dangerous; and 2, to establish a more delicate set of criteria than we have at present for the recognition of early slight injury from lead.

In 1961 Kehoe spoke in a similar vein with a somewhat more hopeful outlook:[115]

> On the purely hypothetical assumption that the lead content of the atmosphere in certain parts (at least) of urban and industrial centres will increase, what then should be the maximum level of such contamination that is compatible with public safety? There is no entirely satisfactory answer to this question at this time. . . . Our investigations have been carried on with this question in mind, however, for many years, and they have now reached a point at which such an answer can be obtained with a fair assurance of its relevance and adequacy, within a reasonable period of time.

One of the more widely known constituents of the air, radioactive material, has a strong hold on public attention and interest, partly from concern. Like so many things, radiation may be a boon or a bane. It is hazardous because it can produce sickness, injury, defects, and death.[116] For present purposes it is solely its hazardous side that will be considered. In its adverse action on the body it has both somatic and genetic effects.

Its injurious effects depend upon the source and nature of the emission and emanation, the level of emission, the age of the subject, the portal of entry or the body area exposed, and the duration and frequency of exposure. High dosage delivered over a brief period may inflict profound injury. In contrast, the consequences of dosage accumulated over a prolonged period from continuous or frequent exposure to low-level irradiation are less precisely and definitely known.[116, 117]

Thresholds do exist for certain effects of radiation such as radiation sickness and death. But there is no evidence that a threshold exists below which no genetic

damage is produced or no delayed somatic effects will appear.[118] Lowest doses tested so far have produced biological damage. No judgment could be more positive or absolute on this point than that pronounced by the United Nations Scientific Committee on the Effects of Atomic Radiation, New York, N. Y. In its report the committee flatly stated: "It is . . . prudent to assume . . . that biological effects will follow irradiation however small its amount." Just as definite is the opinion of the Federal Radiation Council, Washington, D. C., that ". . . any radiation exposure of the population involves some risk; the magnitude of which increases with the exposure."

Our immediate concern is with the hazard of airborne ionizing radiation.[117, 119] Parenthetically it should not be overlooked that dosage from the air may be an addendum to an already existing body burden acquired by other routes. Of the numerous sources of nuclear contamination and exposure the public has been most aware of fallout. In a somber and sobering pronouncement Breslow graphically spelled out the risk and its effects:[120]

> When considering latent effects of contaminating the atmosphere with ionizing radiation, it becomes necessary to recognize that fall-out from a single explosion will persist for decades and its effects will extend over generations. Geneticists agree that the number of mutations—and most of these are harmful—is strictly proportional to the amount of radiation received. There is no "safe" or harmless dose.

Now the public concern over ionizing radiation has extended to include the proposed location of nuclear reactors for power within a city. Less widely mentioned but equally significant is the establishment of nuclear reactors for research by educational institutions.

Reactor installations carry triple jeopardy: possibility of accidents; emission from flues; and disposal of radioactive wastes. To ensure against accidents, controls have been established. But skepticism mingled with concern over the absolute safety of reactors persists. It is not difficult to surmise that operational accidents could still happen from mechanical defects, carelessness, and human error.

Nor is this lingering doubt unfounded. A mishap is a perpetual possibility.[121] Despite controls, accidents have happened. The list is of such length and variety as to be highly impressive.[122] This dismaying number of accidents, the official pronouncement which amounts to a warning that there is no margin of safety, and the easily visualized consequences of nuclear runaway, all these are not exactly reassuring.

For long-range plans in use of nuclear reactors, it is fair to expect that the safety record in operation will improve with practice and experience.

Nor is the possibility of accident the only hazard. An increase in the numbers of nuclear installations has been predicted. With more reactors a rising level of emission products would be expected. As for disposal of nuclear waste materials, it can at several points further increase the hazard of exposure.

To some scientists these considerations are no longer just a scientific question; rather they present a crucial moral issue. According to Beardsley, it has been the policy and practice in public health to eliminate risk for the individual as well as society.[118] There is no selectivity, no preferential choice, no wagering, and no hedging in protecting the health of the public. No level of risk is morally accept-

able. In contrast, he points out, the philosophy of radiation control is based on the principle of accepted risk. It is a calculated risk that has been accepted. A few individuals may be condemned to suffering and premature death in order that certain benefits may accrue to the rest of society.

In radiation control at the policy level, this is a decision that must be faced.

To sum up the yield from experimental studies, these have not yet given complete and decisive information on the essential details of the harmful effects of air pollution. Whether there is a morbid entity or symptom specifically attributable to air pollution is still problematic. There have been few experimental studies to ascertain whether prolonged exposure to low levels of air pollution has cumulative effects as manifested in a chronic process. It is not certain that the complete complex of pollutants responsible for injurious effects of air pollution has been identified.

But there have been gains and advances. Progress is evident in three areas: in showing that the condition of respiratory patients worsens during periods of intensified air pollution and improves in clean air; in identifying potentially dangerous pollutants; and in demonstrating the synergistic action of multiple pollutants.

The Uses of Medical Evidence

The effects of air pollution on health are of more than theoretical interest. True, reduction in air pollution might be desired on grounds other than health. But if the justification for action is based on health, medical evidence is needed.

Then too, the most effective approach to removing or reducing the hazard depends on identifying and defining it. For it is necessary to know what to focus on, and that information also comes from medical evidence.

Most hazards to health from noxious agents are first revealed grossly from their effect at high levels. Usually the presumption of danger from lesser concentrations comes later. From it arises the question: At what level does a pollutant become a menace to health? That also requires medical evidence.

Then comes the search for tolerable, permissible, allowable levels, or, conversely, various thresholds for sickness, injury, defect, and death, each expressed in a definite, mathematical figure. But it is axiomatic in the search for thresholds that the lower the level, the more difficult to establish a critical point. The evidence is likely to be sparse and inconclusive. There are good reasons for this situation in the study of air pollution. There are many variables in both the atmosphere and in individual persons.

After much computation with the variable data, by dint of necessity a figure is usually reached that is in truth an arbitrary approximation. It is equally true to say that often it is an educated estimate.

Sometimes the critical levels of selected pollutants constitute an alert system, or they may be combined to form an index of pollution.

Unlike Los Angeles, New York City does not have at present a system for alerting the population to possible dangers from air pollution episodes. The Department of Air Pollution Control maintains a monitoring system incorporating 30 or more sampling locations throughout the five boroughs. In addition, the Bureau of Air Pollution Control maintains a laboratory on East 121st Street in Manhattan. The laboratory is responsible for analyzing the data supplied by the various sampling stations each of which is charged with responsibility for sampling

certain specific pollutants: smokeshade, dustfall, carbon monoxide, hydrocarbons, oxidants, sulfur dioxide, oxides of nitrogen, and particulate matter.

Since 1964 the Department of Air Pollution Control has been reporting a daily air-pollution index, which is a statistical compilation of readings of sulfur dioxide, carbon monoxide, and particulate matter. The index is calculated by multiplying the sulfur dioxide ppm reading by 10, the smokeshade reading by two, and adding these two totals to the carbon monoxide ppm reading. A 24-hour average—from noon to noon—is then estimated and published as the index for the day. Calculations based on values obtained from 1957 to 1963 led the department to establish the 24-hour average as 12.0.

This index is based on data collected by the Bureau rather than on correlations between concentrations and adverse health effects. Any index value above average is regarded as deleterious.

It has been proposed that this index of air quality be linked with a warning system with four levels of alerts based upon concentration limits of the three pollutants. When these levels are converted to air-pollution indices, the following figures are obtained: air pollution watch at an index of 30; first alert at 39; second alert at 68; and third alert at 90. The Bureau has suggested that an index of 50 for 24 hours be tentatively considered as an adverse air pollution condition for New York City.

Discussion

It is exceedingly difficult to eliminate air pollution entirely from a community or region. It is not, however, unreasonable or impractical to consider purification of the air on a selective basis. To safeguard human health, it must be demonstrated that specific identifiable pollutants are harmful to health. It is also necessary to know the sources of these pollutants and the levels at which they exert irritant or toxic effects.

There has been presented evidence of the effects of air pollution on health and life, obtained from several sources: mortality during episodes of air pollution and mortality rates over longer periods with lesser levels of air pollution; morbidity during critical episodes and morbidity rates over more extended periods with less than episodically high concentrations of air pollution; the concurrent intensification of emphysema in patients during periods of high pollution as well as improvement in their condition when they were protected in rooms filtered from smog; and experimental studies that have demonstrated the injurious effects of several kinds of pollutants on both human beings and animals.

Mortality and morbidity during episodes furnish strong support for a causal relationship between air pollution and injurious effects. It is possible to derive conclusions about such a relationship from data on an acute situation. When all the conditions and circumstances are taken into account, the number of possible causes of the excessive deaths and illnesses becomes narrowed and limited. The nature of the effects as indicated by pathology and symptoms, the presence of pollution in conjunction with stagnation, and its irritant properties, all these concomitants make air pollution the most likely causal agent. The span of time between cause and effect is short. These effects are so large and significant as to be unmistakable. Furthermore, in lieu of experimental induction of injurious

effects in man, the accentuation and improvement in existing disease yields strong corroborative evidence. Indeed, the consistency and coherence of all the other evidence, both in itself and with the acute data, add additional strength to the conclusion of a causal relationship. Thus, the general proposition that air pollution is hazardous does not rest upon a single source of evidence. In its totality, the weight of this consistent and coherent evidence points preponderantly to the conclusion that air pollution is both harmful and lethal, a menace to health and even to life.

But detailed information on the process is much less complete and decisive. Much remains to be known. To learn the pathogenesis of the injurious effects of air pollution and to identify specifically the harmful pollutants, their noxious levels, and their interrelationships, it is necessary to investigate the pollutants singly and in multiple at different levels and for different periods of exposure. This is no small assignment in view of all the other medical and social disorders competing for manpower, financial support, and time. It is small wonder that only a start has been made.

At this time it may not be categorically stated that any particular pollutant is the only harmful one while all others are harmless. Although the identity of the pollutants responsible for deaths and illness during acute episodes has not been absolutely established, evidence from several sources has pointed out potentially dangerous pollutants.

There should be, obviously, an attempt to prevent any further occurrence of episodes of high pollution with their attendant deaths and illness. There should be, also, concern to gain protection against the possible dangers of lesser degrees of pollution that are more generally prevalent. It is a reasonable proposition that substances that are noxious and lethal in high concentrations may exert injurious effects at lesser levels over long periods.

Although it is believed that prolonged exposure to low levels of air pollution is deleterious to health, it may be exceedingly difficult and time-consuming to establish this relationship. Meanwhile, the potential hazard cannot now with certainty be ruled out.

Conclusions

1) Air pollution in episodes of high levels is harmful and can be lethal.

2) Although chronic effects have not yet been demonstrated, it is reasonable to presume that since episodes brought acute sickness and death, exposure to lesser concentrations for prolonged periods will have effects.

3) Not all the injurious pollutants have been identified, nor have their adverse effects been definitely and specifically established.

Recommendations

1) Air pollution should be reduced and abated to safe levels.

2) Since the number and identity of culpable pollutants are not completely known, nor their toxic level definitely established, there should be protection against any pollutant that has been demonstrated to have irritant, noxious, or lethal properties and is therefore potentially dangerous.

3) Since the effect on health of long-continued exposure to low levels of atmospheric pollution is not known, and the chronic process has been presumed

rather than demonstrated, tolerable levels should be protective against not just an acute but also a chronic condition. It is reasonable to presume that substances that are noxious and even lethal in episodes of high concentration may produce injurious effects over longer periods at lower levels. Prudence indicates protection against this possible danger.

4) Research should be vigorously undertaken to establish all the specific pollutants that cause ill health as well as their levels of injurious effect over long periods. At the same time an effort should be made to find evidence of chronic effects. In chronicity it is necessary to know the pathogenic level of each harmful pollutant in order to protect the public not only against acute episodes but against the harmful effects of prolonged exposure to lesser levels.

BIBLIOGRAPHY

1. Firket, J. Sur les causes des accidents survenus dans la vallée de la Meuse, lors des brouillards de décembre 1930, *Bull. Roy. Acad. Med. Belg.* (5 serie) *11*:683-734, 1931.
2. Batta, G., Firket, J., Leclerc, E. *Les Problèmes de l'Atmosphère.* Paris, Masson, 1933.
3. *Air Pollution in Donora, Pa. Preliminary Report,* Public Health Bulletin No. 306, U.S.P.H.S., 1949, 173 pp.
4. *Mortality and Morbidity during London Fog of December 1952.* Report on public health and medical subjects, No. 95. London. Ministry Health, 1954, 60 pp.
5. Greenburg, L., Jacobs, M. B., Drolette, B. M., Field, F. and Braverman, M. M. Report of an air pollution incident in New York City, November 1953. *Public Health Rep. 77*:7-16, 1962.
6. Greenburg, L. Data presented at the 58th Annual Meeting of the Air Pollution Control Association, Toronto, Canada, June 22, 1965. *New York World-Telegram and Sun,* June 22, 1965.
7. Lawther, P. J. Air pollution, *Bull. N.Y. Acad. Med. 41*:214-17, 1965.
8. Brodie, F. J. Some remarkable features in the winter of 1890-1891, *Quart. J. Roy. Meteorol. Soc. 17*:155-67, 1891.
9. Brodie, F. J. On the prevalence of fog in London during the 20 years 1871-1890, *Quart. J. Roy. Meteorol. Soc. 18:* 40-45, 1892.
10. Russell, W. T. Influence of fog on mortality from respiratory diseases, *Lancet 2*:335-39, 1924.
11. Logan, W. P. D. Mortality from fog in London, January, 1956, *Brit. Med. J. 4969*:722-25, 1956.
12. Parker, A. Air pollution research and control in Great Britain, *Amer. J. Public Health 47*:559-69, 1957.
13. Burgess, S. G. and Shaddick, C. W. Bronchitis and air pollution, *Roy. Soc. Health J. 79*:10-24, 1959.
14. Hewitt, D. Mortality in London boroughs, 1950-1952, with special reference to respiratory disease, *Brit. J. Prev. Soc. Med. 10*:45-57, 1956.
15. Pemberton, J. and Goldberg, C. Air pollution and bronchitis, *Brit. Med. J. 4887*:567-70, 1954.
16. Daly, C. Air pollution and causes of death, *Brit. J. Prev. Soc. Med. 13*:14-27, 1959.
17. Stocks, P. Cancer and bronchitis mortality in relation to atmospheric deposit and smoke, *Brit. Med. J. No. 5114*:74-79, 1959.
18. Gorham, E. Bronchitis and the acidity of urban precipitation, *Lancet 2*:691, 1958.
19. Fairbairn, A. S. and Reid, D. D. The natural history of chronic bronchitis, *Lancet 1*:1147-52, 1954.
20. Ryder, C. F. Chronic respiratory diseases, a mushrooming challenge. *Second A.M.A. Annual Congress on Environmental Health Problems,* Chicago, April 26, 1965. U.S. Dept. of Health, Education, and Welfare, Pub. Health

Serv., Div. of Air Pollution, 1965, 8 pp.

21. Mills, C. A. Respiratory and cardiac deaths in Los Angeles smogs, *Amer. J. Med. Sci. 233*:379-85, 1957.
22. Winkelstein, W. Air pollution and mortality in Erie County, N. Y. In: *The Allergic Patient,* New York, Winthrop Labs., 1966.
23. Phelps, H. W., Sobel, G. W. and Fisher, N. E. Air pollution asthma among military personnel in Japan, *J.A.M.A. 175*:990-93, 1961.
24. Davenport, S. J. and Morgis, G. G. *U.S. Bureau of Mines Bulletin 537,* 1954, 448 pp.
25. Firket, J. Sur les causes des accidents survenus dans la vallée de la Meuse, lors des brouillards de décembre 1930. *Bull. Roy. Acad. Med. Belg.* (5 serie) *11*:683-741, 1931.
26 Ashe, W. F. Acute effects of air pollution in Donora, Pa. In: *Air Pollution.* Proceedings of the U.S. Technical Conference on Air Pollution, New York, McGraw-Hill, 1952, pp. 455-61.
27. Wilkins, E. T. Air pollution and the London fog of December 1952, *J. Roy. San. Inst. 74*:1-15, 1954.
28. Greenburg, L., Field, F., Reed, J. I. and Erhardt, C. I. Air pollution and morbidity in New York City, *J.A.M.A. 182*:161-64, 1962.
29. Greenburg, L., Erhardt, C., Field, F., Reed, J. I. and Seriff, N. S. Intermittent air pollution episode in New York City, 1962, *Public Health Rep. 78*:1061-64, December 1963.
30. Ciocco, A. and Thompson, D. J. A follow-up of Donora ten years after: methodology and findings, *Amer. J. Public Health 51*:155-64, 1961.
31. Pemberton, J. Air pollution as possible cause of bronchitis and lung cancer, *J. Hyg. Epidem.* (Praha) *5*:189-94, 1961.
32. Fletcher, C. M. Disability and mortality from chronic bronchitis in relation to dust exposure, *A.M.A. Arch. Industr. Health 18*:368-73, 1958.
33. Farber, S. M. and Wilson, R. H. Pulmonary emphysema, *Ciba Clin. Symposia 10*:171-205, 1958.
34. Motley, H. L. Pulmonary emphysema, *Missouri Med. 57*:701-09, 1960.
35. Fletcher, C. M. Chronic bronchitis, its prevalence, nature and pathogenesis, *Amer. Rev. Resp. Dis. 80*:483-94, 1959.
36. Reid, D. D. Environmental factors in respiratory disease, *Lancet 1*:1289-94, 1958.
37. Fairbairn, A. S., and Reid, D. D. Air pollution and other local factors in respiratory disease, *Brit. J. Prev. Soc. Med. 12*:94-103, 1958.
38. Holland, W. W., Spicer, C. C. and Wilson, J. M. G. Influence of weather on respiratory disease, *Lancet 2*:338-41, 1961.
39. Dohan, F. C. Air pollutants and incidence of respiratory disease, *Arch. Environ. Health 3*:387-95, 1961.
40. Skalpe, I. O. Long-term effects of sulphur dioxide exposure in pulp mills, *Brit. J. Industr. Med. 21*:69-73, 1964.
41. Lewis, R., Gilkeson, M. M. and McCaldin, R. O. Air pollution and New Orleans asthma. A preliminary report, *Public Health Rep. 77*:947-54, 1962.
42. Zeidberg, L. D., Prindle, R. A. and Landau, E. Nashville air pollution study. I. Sulfur dioxide and bronchial asthma. A preliminary report, *Amer. Rev. Resp. Dis. 84*:489-503, 1961.
43. National conference on air pollution, *Public Health Rep. 78*:423-29, 1963.
44. *Clean Air for California: Initial Report, Air Pollution Study Project,* Sacramento, State of Calif. Dept. Public Health, March, 1955.
45. McCarroll, J. R., Cassell, E. J., Ingram, W., and Wolter, D. Health and the urban environment: Health profiles versus environmental pollutants, *Amer. J. Public Health 56*:266-75, 1966.
46. Cassell, E. J., McCarroll, J. R., Ingram, W. and Wolter, D. Health and the urban environment: Air pollution and family illness. III. Two acute air pollution episodes in New York City: Health effects. *Arch. Environ. Health 10*:367-69, 1965.
47. McCarroll, J. R., Cassell, E. J., Wolter, D. W., Mountain, J. D., Diamond, J. R. and Mountain, I. M. Air pollution and illness in smokers and nonsmokers, *A.M.A. Air Pollution Medical*

Conference, March 2-4, 1966, Los Angeles, Calif.

48. Motley, H. L. Use of pulmonary function tests for disability appraisal: including evaluation standards in chronic pulmonary disease, *Dis. Chest 24:* 378-89, 1953.
49. Motley, H. L. Clinical pulmonary physiology. *Industr. Med. and Surgery 22:*262-67, 1953.
50. Spicer, W. S., Sr. Complexity of the relationship between air pollution and respiratory health. In: *National Conference on Air Pollution,* Public Health Serv., Div. of Air Pollution, Washington, D.C. 1963, Public Health Service Publication 1022, pp. 136-38.
51. Prindle, R. A., Wright, G. W., McCaldin, R. O., Marcus, S. C., Lloyd, T. C. and Bye, W. E. Comparison of pulmonary function and other parameters in two communities with widely different air pollution levels, *Amer. J. Public Health 53:*200-17, February, 1963.
52. Waller, R. E. and Lawther, P. J. Some observations on London fog, *Brit. Med. J. 2:*1356-58, Dec. 3, 1955.
53. Waller, R. E. and Lawther, P. J. Further observations on London fog, *Brit. Med. J. 2:*1473-75, Dec. 21, 1957.
54. Farber, S. M., and Wilson, R. H. L. Air contamination: A respiratory hazard, *J.A.M.A. 180:*362-66, 1962.
55. Motley, H. L., Smart, R. H. and Leftwich, C. I. Effect of polluted Los Angeles air (smog) on lung volume measurements, *J.A.M.A. 171:*1469-77, 1959.
56. Heimann, H. Effects of air pollution on human health. In: *Air Pollution,* World Health Organization Monograph Series 46, U.S. ed. New York, Columbia Univ. Press, 1961, pp. 158-220.
57. *Industrial Hygiene and Toxicology,* 2d rev. ed. Frank A. Patty, ed., vol. 2. David W. Fassett and Don D. Irish, eds. New York, Interscience, 1949, p. 895.
58. Lawther, P. J. Effects of inhalation of sulphur dioxide on respiration and pulse rate in normal subjects, *Lancet 2:*745-48, 1955.
59. Greenwald, I. Effects of inhalation of low concentrations of sulfur dioxide upon man and other mammals, *A.M.A. Arch. Industr. Hyg. Occup. Med. 10:* 455-75, 1954.
60. Frank, R., quoted in: Research in air pollution. Conference Report, Third Air Pollution Research Seminar, March 22-24, 1960, New Orleans, *Public Health Rep. 75:*1173-89, 1960.
61. Frank, N. R., Amdur, M. O., Worcester, J. and Whittenberger, J. L. Effects of acute controlled exposure to SO_2 on respiratory mechanics in healthy male adults, *J. Appl. Physiol. 17:*252-58, 1962.
62. Amdur, M. O. Toxicological studies of air pollutants, *Public Health Rep. 69:* 724-26, 1954.
63. Cralley, L. V. The effect of irritant gases upon the rate of ciliary activity, *J. Industr. Hyg. Tox. 24:*193-98, 1942.
64. Kotin, P. and Falk, H. The deposition of carcinogen-bearing particulate matter in the tracheo-bronchial tree in relation to particle size and effect of air pollutants and tobacco smoke on ciliary activity and mucus secretion of the respiratory epithelium, *Proc. Amer. Ass. Cancer Res. 2:*127-28, 1956.
65. Dalhamn, T. Mucous flow and ciliary activity in the trachea of healthy rats and rats exposed to respiratory irritant gases (SO_2, NH_3, HCHO), *Acta Physiol. Scand. 36:* (suppl.), 123, 1956, 161 pp.
66. Dalhamn, T., and Rhodin, J. Mucous flow and ciliary activity in the trachea of rats exposed to pulmonary irritant gas, *Brit. J. Industr. Med. 13:*110-13, 1956.
67. van Wijk, A. M. and Patterson, H. S. Percentage of particles of different sizes removed from dust-laden air by breathing, *J. Industr. Hyg. Tox. 22:* 31-35, 1940.
68. Brown, J. H., Cook, K. M., Ney, F. G. and Hatch, T. Influence of particle size upon the retention of particulate matter in the human lung, *Amer. J. Public Health 40:*450-80, 1950.
69. Dautrebande, L. and Capps, R. Studies on aerosols. IX. Enhancement of irri-

tating effects of various substances on the eye, nose, and throat by particulate matter and liquid aerosols in connection with pollution of the atmosphere. *Arch. Int. Pharmacodyn. 82:*505-28, 1950.

70. Dautrebande, L., Shaver, J. and Capps, R. Studies on aerosols. XI. Influence of particulate matter on the eye irritation produced by volatile irritants and importance of particle size in connection with atmospheric pollution. *Arch. Int. Pharmacodyn. 85:*17-48, 1951.
71. Stokinger, H. E., Steadman, L. T., Wilson, H. B., Sylvester, G. E., Dziuba, S., and LaBelle, C. W. Lobar deposition and retention of inhaled insoluble particulates, *Arch. Industr. Hyg. and Occup. Med. 4:*346-53, 1951.
72. LaBelle, C. W., Long, J. E., and Christafano, E. E. Synergistic effects of aerosols. *Arch. Industr. Health 11:* 297-304, 1955.
73. Hemeon, W. C. L. Estimation of health hazards from air pollution. *Arch. Industr. Health 11:*397-402, 1955.
74. Palm, P. E., McNerney, J. M., and Hatch, T. Respiratory dust retention in small animals, *Arch. Industr. Health 13:*355-65, 1956.
75. Amdur, M. O. Influence of aerosols upon the respiratory response of guinea pigs to sulfur dioxide, *Amer. Industr. Hyg. Ass. Quart. 18:*149-55, 1957.
76. Sim, V. M. and Pattle, R. E. Effect of possible smog irritants on human subjects, *J.A.M.A. 165:*1908-13, 1957.
77. Mitchell, R. I. Retention of aerosol particles in the respiratory tract, *Amer. Rev. Resp. Dis. 82:*627-39, 1960.
78. Boren, H. G. Carbon as a carrier mechanism for irritant gases, *Arch. Environ. Health 8:*119-24, 1964.
79. Schepers, G. W. H. Air pollution: particulate matter. In: Symposium on Medical Aspects of Air Pollution. *American College of Chest Physicians, June 24, 1961,* New York City.
80. Treon, J. F., Dutra, F. R., Cappel, J., Sigmon, H. and Younker, W. Toxicity of sulfuric acid mist, *Arch. Industr. Hyg. Occup. Med. 2:*716-34, 1950.
81. Amdur, M. O., Schulz, R. Z. and Drinker, P. Toxicity of sulfuric acid mist to guinea pigs, *Arch. Industr. Hyg. Occup. Med. 5:*318-29, 1952.
82. Amdur, M. O., Silverman, L. and Drinker, P. Inhalation of sulfuric acid mist by human subjects, *Arch. Industr. Hyg. Occup. Med. 6:*305-13, 1952.
83. Pattle, R. E., Burgess, F. and Cullumbine, H. The effects of a cold environment and of ammonia on the toxicity of sulphuric acid mist to guinea-pigs, *J. Path. Bact. 72:*219-32, 1956.
84. Pattle, R. E. and Cullumbine, H. Toxicity of some atmospheric pollutants, *Brit. Med. J. 2:*913-16, Oct. 20, 1956.
85. Corn, M. and DeMaio, L. Sulfate particulates: size distribution in Pittsburgh air, *Science 143:*803-04, Feb. 21, 1964.
86. Amdur, M. O. Effects of a combination of SO_2 and H_2SO_4 on guinea pigs, *Public Health Rep. 69:*503-06, 1954.
87. Ellis, B. A. Report on the determination of sulphur gases in air. Appendix I, pp. 38-39. In: *The Investigation of Atmospheric Pollution,* Report on Observations in the Year Ended 31st March, 1931, Seventeenth Report, Department of Scientific and Industrial Research, His Majesty's Stationery Office, London, 1931.
88. Magill, P. L. and Benoliel, R. W. Air pollution in Los Angeles County. Contribution of Combustion Products, *Industr. Eng. Chem. 44:*1347-51, 1952.
89. Haagen-Smit, A. J. Chemistry and physiology of Los Angeles smog, *Industr. Eng. Chem. 44:*1342-46, 1952.
90. Haagen-Smit, A. J. and Fox, M. M. Ozone formation in photochemical oxidation of organic substances, *Industr. Eng. Chem. 48:*1484-87, 1956.
91. Haagen-Smit, A. J., Bradley, C. E. and Fox, M. M. Ozone formation in photochemical oxidation of organic substances, *Industr. Eng. Chem. 45:* 2086-89, 1953.
92. Mader, P. P., MacPhee, R. D., Lofberg, R. T. and Larson, G. P. Composition of organic portion of atmospheric aerosols in the Los Angeles area, *In-*

*dustr. Eng. Chem. 44:*1352-55, 1952.

93. Blacet, F. E. Photochemistry in the lower atmosphere, *Industr. Eng. Chem. 44:*1339-42, 1952.
94. Prindle, R. A. and Landau, E. Health effects from repeated exposures to low concentrations of air pollutants, *Public Health Rep. 77:*901-09, 1962.
95. Murphy, S. D., Leng, J. K. and Ulrich, C. E. Effects of diluted auto-exhaust on pulmonary function of guinea pigs, *Pharmacologist 3:*61, 1961.
96. Ehrlich, R. Effect of air pollutants on respiratory infection, *Arch. Environ. Health 6:*638-42, 1963.
97. Kleinerman, J. and Wright, G. W. The reparative capacity of animal lungs after exposure to various single and multiple doses of nitrite, *Amer. Rev. Resp. Dis. 83:*423-24, 1961.
98. Freeman, G. and Haydon, G. B. Emphysema after low-level exposure to NO_2, *Arch. Environ. Health 8:*125-28, 1964.
99. Griswold, S. S., Chambers, L. A. and Motley, H. L. Report of a case of exposure to high ozone concentrations for two hours, *Arch. Industr. Health 15:*108-10, 1957.
100. Stokinger, H. E., Wagner, W. D. and Dodbrogorski, O. J. Ozone toxicity studies. III. Chronic injury to lungs of animals following exposure at a low level, *Arch. Industr. Health 16:* 514-22, 1957.
101. Purvis, M. R., Miller, S. and Ehrlich, R. Effect of atmospheric pollution on susceptibility to respiratory infection. I. Effect of ozone, *J. Infect. Dis. 109:* 238-42, 1961.
102. Kotin, P. and Falk, H. L. Air pollution and lung cancer. In: *National Conference on Air Pollution,* Public Health Serv., Div. of Air Pollution, Washington, D.C., 1963, Public Health Service Publication 1022, pp. 140-42.
103. Wynder, E. L. and Hoffmann, D. Air pollution and lung cancer, *Ibid.,* pp. 143-48.
104. Sayers, R. R. and Davenport, S. J. *Review of Carbon Monoxide Poisoning.* Public Health Bull. No. 195, Washington, D.C., Govt. Print. Office, 1930, 97 pp.
105. Gettler, A. O. and Mattice, M. R. "Normal" carbon monoxide content of the blood, *J.A.M.A. 100:*92-97, 1933.
106. Sayers, R. R., Yant, W. P., Levy, E. and Fulton, W. B. *Effect of Repeated Daily Exposure of Several Hours to Small Amounts of Automobile Exhaust Gas.* Public Health Bulletin 186, Washington, D.C., Govt. Print. Office, 1929, 58 pp.
107. Sievers, R. F., Edwards, T. I., Murray, A. L. and Schrenk, H. H. Effect of exposure to known concentrations of carbon monoxide, *J.A.M.A. 118:*585-88, 1942.
108. Sievers, R. F., Edwards, T. I., and Murray, A. L. *A Medical Study of Men Exposed to Measured Amounts of Carbon Monoxide in the Holland Tunnel for 13 Years.* Pub. Health Serv., Public Health Bulletin 278, Washington, D.C., Govt. Print. Office, 1942. 74 pp.
109. Hofreuter, D. H., Catcott, E. J. and Xintaras, C. Carboxyhemoglobin in men exposed to carbon monoxide, *Arch. Environ. Health 4:*81-85, 1962.
110. Schulte, J. H. Effects of mild carbon monoxide intoxication, *Arch. Environ. Health 7:*524-30, 1963.
111. Ayres, S. M., Giannelli, Jr., S. and Armstrong, R. G. Carboxyhemoglobin: hemodynamic and respiratory responses to small concentrations, *Science 149:*193-94, 1965.
112. Kehoe, R. A., Thamann, F., and Cholak, J. Lead absorption and excretion in relation to the diagnosis of lead poisoning, *J. Industr. Hyg. 15:*320-40, 1933.
113. Working Group on Lead Contamination. *Survey of Lead in the Atmosphere of Three Urban Communities.* U.S.P.H.S., Division of Air Pollution, Public Health Service Publication 999-AP-12.
114. Minot, A. S. Physiological effects of small amounts of lead: An evaluation of the lead hazard of the average individual, *Physiol. Rev. 18:*554-77, 1938.
115. Kehoe, R. A. Present hygienic problems relating to the absorption of lead, *J. Roy. Inst. Public Health and Hyg. 24:*177-203, 1961.

116. Crow, J. F. Effects of Radiation and Fallout, Pamphlet 256, Public Affairs Committee, Inc. Oct. 1957, 28 pp.
117. Symposium on Today's Medical Problems in Ionizing Radiation. *Bull. N.Y. Acad. Med. 38*:727-55, 1962.
118. Beardsley, E. E. Radiation Control. The scientific, ethical, and historical background of a problem facing American society today, *Natur. Philosopher 1*:3-80, 1963.
119. Davies, S. Man's newest health problem . . . ionizing radiation, *Health News 41*:15-19, 1964.
120. Breslow, L. Health effects of air pollution, *Amer. J. Public Health 48*:913-17, 1958.
121. U.S. Atomic Energy Commission. *Theoretical Possibilities and Consequences of Major Accidents in Large Nuclear Power Plants.* Washington, D.C., Govt. Print. Office, 1957.
122. U.S. Atomic Energy Commission, Division of Operational Safety. *Operational Accidents and Radiation Exposure Experience within the U.S. Atomic Energy Commission, 1943-1964.* Washington, D.C., Govt. Print. Office, 1965.